

public for funds with which to propagate themselves. Every five-hundredth person, including men, women and children, in California is an educated doctor of medicine whose office is the only kind of health center our people need. Why centralize groups of them—these same doctors—in “health centers” with expensive overhead that the public must support?

EPHEDRINE, A PROMISING THERAPEUTIC AGENT

Tasted by the Emperor Shen Nung about 5100 years ago and placed by him in the “medium class,” and described by Li Shih Cheng in 1596 A. D. as a diaphoretic, circulatory stimulant, antipyretic, cough sedative, etc., ephedrine emerged from seclusion in 1887, though really its possibilities have been fully revealed only within the last two years. Ephedrine is the active alkaloid of Ma Huang, or *Ephedra vulgaris* var. *helvetica*, closely resembling epinephrine in its actions qualitatively, but differing quantitatively and in some other important particulars. Recent studies of the drug, which is an ingredient of many famous Chinese prescriptions, have been made by the Chinese pharmacologist, K. K. Chen, and by Chen and Schmidt of the Peking Union Medical College. Fortunately, the results of a very recent clinical study made by Miller of the University of Pennsylvania Hospital, supported by the Council of Pharmacy and Chemistry of the American Medical Association, parallel and confirm those of the animal work by Chen and his associates. The promising therapeutic usefulness of ephedrine and its advantages over epinephrine merit attention at this time, though undoubtedly further and extended clinical trial, which is promised by Miller and others, will finally determine its place in the therapeutic armamentarium.

The crude drug, *Ephedra vulgaris*, yields two alkaloids, namely, ephedrine and pseudo-ephedrine, the latter being isomeric with ephedrine and their physiological actions are identical. Ephedrine was first isolated by Nagai in 1887. Its formula is $C_{10}H_{15}N$, and chemically it is stated to be phenyl 1-ol 1-methyl 2-methylamine 2-ethane. Its salts crystallize well and dissolve in water. According to Chen and Schmidt, the watery solutions remain active after exposure to air and light for forty-five days. The solutions remain colorless and can be boiled without loss of activity. There is no doubt, therefore, that ephedrine is more stable than epinephrine and this is a decided advantage. Its greater stability in vitro suggests at once that its pharmacological actions would be more lasting than those of epinephrine, and this was found to be the case in the careful and extensive studies of Chen and Chen and Schmidt.

The outstanding effect in animals, according to these investigators, is circulatory stimulation, characterized by marked cardiac acceleration and a sustained rise of blood pressure lasting 30 minutes and longer. The cardiac acceleration is due to stimulation of the stellate ganglia and the accelerator endings, for the drug stimulates the heart when it is applied locally to the stellate ganglion, and also when perfused through excised hearts. With moder-

ate doses, the heart volume is increased and the rate slowed as the maximal level of blood pressure is reached, thus resulting in an increased output of blood from the heart. With high doses and concentrations the heart is depressed and finally stops from direct paralysis by the drug, though the stoppage is usually preceded by fibrillation. As a result of the increased cardiac output, the diuresis later is increased, though in the beginning it is decreased owing to the marked constriction of renal vessels. The renal vessels share in the vasoconstriction of splanchnic vessels in general, and this peripheral constriction is largely responsible for the initial rise of blood pressure produced by the drug, but later the cardiac acceleration outlasts the vascular constriction and, hence, the sustained pressure is largely cardiac. The vessels of the extremities are much less constricted, the coronary vessels being dilated and the pulmonary, unaffected. Atropine and section of the vagi do not prevent the circulatory effects, and, hence, they are of sympathetic origin.

Other effects are inhibition of the intestine, stimulation of the uterus, relaxation of constricted bronchi, mydriasis lasting about one hour, and increase of salivary, sweat, lymph and gastric secretions. Pancreatic, biliary, and intestinal secretions are unaffected. In man, slight sweating without nausea occurs after taking 0.06 gm. by mouth. The drug cannot be detected in the urine after daily intravenous doses in rabbits, and is presumably destroyed slowly. In a study of twenty-two dogs suffering from different kinds of shock and hemorrhage with low blood pressures, Chen found that 2 to 3 mgms. per kilo of ephedrine intravenously promptly raised the blood pressures. The beneficial effects in anaphylactic shock lasted not longer than one hour and in all other shock conditions for about, or not over, three hours. The drug was ineffective when the pulse was imperceptible, the blood pressure was low for long periods, respiration ceased, and when hemorrhage exceeded 25 per cent. Chen thinks ephedrine breaks the vicious circle of shock, bringing more nutrition to the heart itself, the medulla and other organs, the pulse rate being invariably increased in the shock conditions. He feels it could be used beneficially in surgical shock and hemorrhage.

According to Chen, the toxicity of ephedrine is rather low. The minimum fatal dose intravenously for rabbits, cats and dogs is about 0.07 gm. per kilo. In rabbits, the fatal dose by mouth is 0.6 gm., intramuscularly, 0.34 gm., hypodermically, 0.36 gm. and intraperitoneally, 0.39 gm. per kilo. Convulsions occur only on intravenous injection, and death is due to cardiac stoppage. Recovery from sublethal doses is complete. The ordinary effects of ephedrine can be demonstrated in animals with doses of from 0.25 to 0.5 mgm. per kilo intravenously; and also from 10 mgms. hypodermically or 25 mgms. per kilo into the intestine. In man, 40 to 100 mgms. by mouth cause a definite rise of blood pressure and decrease in pulse rate, the effects beginning in thirty minutes and persisting more than two hours. This result in man has been fully confirmed by Miller. As for the animal studies, the work of Chen and Chen and Schmidt proves conclusively that ephedrine, just like epinephrine, is a sympathomimetic drug, and that it has distinct advantages over epi-

nephrine, namely, that its actions are more prolonged, those of epinephrine being fleeting, and that it is effective by mouth, while epinephrine is not.

The equally good results of Miller in the clinic deserve mention. Miller administered from 0.05 to 0.125 gm. ephedrine sulphate orally or hypodermically to eighty-four patients under controlled conditions. There were no unfavorable phenomena, the patients did not object to taking the drug, and some felt better. The most consistent change was in the systolic blood pressure, elevations occurring in seventy out of eighty-four instances, and amounting to from 10 to 40 or more millimeters of mercury. In thirteen cases no rise of blood pressure occurred, and in six there was an actual fall. The rise reached the highest level within from one to two hours, and then the pressure fell slowly during three or more hours to the original level. The blood pressure rises after oral administrations were about as marked as after the hypodermic, but the action was more prompt after the hypodermic injection. In most cases the pulse rate was slowed, due probably to reflex stimulation of the vagus center from the high blood pressure, and a compensatory phenomenon. X-ray showed the excursions of the ventricles and aortic shadows to be greater than before. The pulse was more forceful and the heart sounds were louder. All of these changes are strictly consistent with those found by Chen and Schmidt in animals. Presumably, the cardiac output is also increased in man and the diuresis, though variable, tended to be increased, according to Miller. Albuminuria occurred in patients with increased blood pressure, and whether there was an irritation of the kidney by the drug or not is not settled. The basal metabolism was increased in two out of four cases, but hyperglycemia was absent.

Important effects were observed on the nasal mucosa. The application of a 5 per cent solution of ephedrine sulphate contracted the turbinates in two and one-third minutes in all seventeen cases tested. The mucosa appeared thin and seemed to fit closer to the bone; the color was pale, but not as anemic as after epinephrine. Relaxation began at the end of two hours and thirty-five minutes. No irritation was present, such as occurs with epinephrine.

In certain disease conditions, Miller obtained definite benefits from ephedrine. Oral administration gave temporary improvement in two cases of Addison's disease, the paroxysmal attacks of a number of cases of asthma were relieved more efficiently than with epinephrine, the subjective sensations of urticaria were relieved, and there was marked temporary improvement in circulatory collapse. Miller concludes that the widest range of therapeutic usefulness of ephedrine will be in the treatment of asthma, hypotension and acute circulatory depression, and in certain congestive nasal conditions. A distinct advantage over epinephrine is suggested in the local treatment of nasal conditions, in nasal sprays for hay-fever, sinusitis, and perhaps as an aid in operations on the nose, etc. Other advantages over epinephrine have been pointed out above.

Thus, it appears that the newer methods of experimentation confirm, extend and rationalize the effects and uses of an ancient drug understood in

a general way and used quite intelligently, though empirically, by the Chinese thousands of years ago. We should be thankful for this belated knowledge, as indeed many a patient may be ultimately grateful to the possibilities that ephedrine holds out. It may be hoped that not only Chinese materia medica, but also that of other oriental and other countries, end even of California, whose medicinal plants have not yet been investigated, will furnish remedies as promising as ephedrine.

Chen and Schmidt: J. Pharm. Exp. Therap., 1924, 24: 339. "The Action of Ephedrine, the Active Principle of the Chinese Drug Ma Huang."

Chen: Proc. Soc. Exp. Biol. Med., 1925, 22:404. "The Acute Toxicity of Ephedrine."

Chen: Proc. Soc. Exp. Biol. Med., 1925, 22:568. "The Effect of Repeated Administration of Ephedrine."

Chen: Proc. Soc. Exp. Biol. Med., 1925, 22:570. "The Effect of Ephedrine on Digestive Secretions."

Chen: J. Am. Pharm. Assoc., 1925, 14:189. "A Pharmacognostic and Chemical Study of Ma Huang (*Ephedra vulgaris* var. *Helvetica*)."

Chen: J. Pharm. Exp. Therap., 1925, 26:83. "The Effect of Ephedrine on Experimental Shock and Hemorrhage."

Miller: Am. J. Med. Sci., 1925, 170: 157. "A Consideration of the Clinical Value of Ephedrine, With a Report on Its Effects in Certain Special Cases."

"THE WAY OF THE TRANSGRESSOR IS HARD"

The tragedy of the Murphy Memorial Hospital, now a familiar story to readers of hospital and health literature around the world, is at last revealing itself in all of its sordidness to the people of the beautiful little city of Whittier, California. Once the Murphy Memorial was a beautiful, well appointed, properly conducted hospital, pointed to with pride by physicians, hospital organizations and intelligent people everywhere. It was rated high in hospital directories as a scientific, health-serving institution and was rendering splendid service to a community much in need of such facilities.

Then certain cults and their cronies of the licensed medical profession got together, put on a referendum and not only *repudiated* a written agreement between the community and Colonel Simon J. Murphy, the benefactor who built and donated the hospital to the people, but what was even worse, *if possible*, they succeeded in "*opening*" the hospital as a place for all and sundry to practice their "systems" on those who might be credulous enough to trust their health in such circumstances. After all available means had been employed, without success, to save the situation, the Council on Medical Education and Hospitals of the American Medical Association and the American College of Surgeons removed the hospital from the accredited lists and it was dropped from all hospital directories of standing. The American Hospital Association dropped it from membership. The cultists and their followers were jubilant and broadcast their happiness and, unfortunately for them, their prophecies also.

WHAT HAPPENED

Politics, cultism and sciosophy generally have had full swing now for some five months. During that time the city council and their hospital board have quite thoroughly demonstrated every argument and